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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,039	09/23/2002	Ivars Kalvins	81847	9469
23685	7590	06/24/2004	EXAMINER	
KRIEGSMAN & KRIEGSMAN 665 FRANKLIN STREET FRAMINGHAM, MA 01702			SACKEY, EBENEZER O	
			ART UNIT	PAPER NUMBER
			1626	

DATE MAILED: 06/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,039	KALVINS ET AL.	
	Examiner	Art Unit	
	EBENEZER SACKKEY	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 March 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 9-10 and 12-14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4,9,13 and 14 is/are rejected.
- 7) ☒ Claim(s) 3,5,10 and 12 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>3/31/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This is in response to applicant's amendment filed on 03/31/04

Status of Claims

Claims 1-5, 9-10 and 12-14 are pending.

Amendments:

Cancelled claims: 6-8 and 11.

Amended claims: 1-5, 9-10.

New claims: 12-14.

Remarks:

(a) Rejection under 35 USC 112, second paragraph (indefiniteness):

The rejection of claims 1-2 and dependent claims 3-4 as to the word "residue" has been overcome by the amendment to the claims by reciting the phrase "selected from the group consisting of".

(b) Rejection under 35 USC 101 (use of):

The cancellation of claims 8 and 11 and the amendment of claims 9 and 10 has overcome the rejection under 35 USC 101.

Maintained rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2 and 4 remain rejected under 35 U.S.C. 102(b) as being anticipated by Eremeev et al., and CA: DN 115:48589 for the reasons set forth in the previous office action mailed on 09/29/03.

Applicants claim relate to aziridine-1-hydroxymethyl compounds of formula (I). Eremeev et al., anticipate the genus of amended claim 1, wherein R is a bond and n is 2 and each of R₁ and R₂ is H or CH₃. See compounds IV and IX on page 369.

New Objections:

The amendment filed on 03/31/04 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: "--and a linker moiety capable of bonding--"(claim 1); "a linker moiety that is a divalent radical, derived from a molecule" (claims 2 and 3) and new claim 14 "---said linker moiety is substituted with at least one substituents selected from the group consisting of cyano, hydroxy, lower C₁₋₆alkyl, lower C₁₋₆alkoxy---"

Applicant is required to cancel the new matter in the reply to this office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 9 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for tumors or cancerous diseases such as Colon, Stomach, Lung, Breast, Kidney and Uterus, does not reasonably provide enablement for tumors and cancerous diseases in general. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The treatment of tumors or cancerous diseases in general is not properly supported in the specification. The specification fails to adequately teach how to use the invention properly by failing to provide enabling disclosure regarding the above diseases. Because of the high level of unpredictability associated with chemical or biological systems, a greater amount of evidentiary support is needed in order to fully satisfy the requirement of 35 USC 112, first paragraph, that applicants provide sufficient guidance as regards "how to use" the invention. For example, what is encompassed by "tumors or cancerous diseases"?

It is noted that applicants have provided antitumoral activity data pursuant to cytotoxicity test on pages 10-11. However, the claim is extremely broad due to the vast number of possible tumors and cancerous diseases encompassed by the claim.

Applicants need to point out in the specification where there is support including pharmaceutical data for all the alleged utility. A mere statement does not provide enabling support for such a utility or limit the claim to diseases found in Table 1 of the specification.

It is the state of the art that there is no known cure for tumors or cancerous diseases in general. Chemotherapeutic agents are frequently useful against a specific

neoplasm or cancer and especially with the unpredictability of in the state of the art, there are no drugs broadly effective against all forms of cancer. See Carter, S. K. et al., *Chemotherapy of Cancer*; Second Edition; John Wiley & Sons: New York 1981; Appendix C.

Thus, in the absence of a showing of correlation between tumors or cancerous diseases claimed as capable of treatment by compounds of formula (I), one of ordinary skill in the art is unable to fully predict possible results from the administration of the compounds of claim 1 due to the unpredictability of most treatments.

Inventions targeted for human therapy bear a particular heavy responsibility to provide supporting data because of the unpredictability in biological responses to therapeutic treatment. Also, the standard of enablement is higher of such inventions simply because effective treatments for disease conditions are relatively rare, and may be prima facie unbelievable in the absence of strong supporting data. See *Ex parte Stevens*, 16 USPQ 2nd 1379 (BPAI) in which a prima facie case of nonenablement against a method of treating cancer was affirmed based solely on legal precedents. See also *Ex Parte Chwang*, 231 USPQ 751 (BPAI) 1986 and *Ex Parte Krepelka*, 231 USPQ 746 (BPAI) 1986.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13 and 14 recite the limitation "—is substituted with at least one substituents selected from the group consisting of cyano, hydroxy, lower C₁₋₆alkyl, lower

C₁₋₆alkoxy, nitro, amino, monosubstituted amino, trihaloalkyl and halogen groups" in lines 1-3. There is insufficient antecedent basis for this limitation in the claim.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to E. Sackey whose telephone number is (703) 305-6889. The examiner can normally be reached on Monday-Friday from 7:30 am to 4:30 pm.

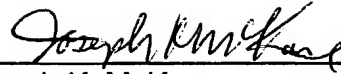
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane, can be reached on (703) 308-4537. The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Art Unit: 1626

EOS

June 16, 2004

A handwritten signature in cursive script, reading "Joseph K. McKane", written in black ink.

Joseph K. McKane
Supervisory Patent Examiner
Art Unit 1626, Group 1600
Technology Center 1